

Amendments to the Specification

(Underline indicates text inserted, Strike-through indicates text deleted)

On page 1, line 1, please replace the current title with the following rewritten title:

ANTIBODIES TO G-PROTEIN PARATHYROID HORMONE RECEPTOR HLTDG74

On page 6, please replace the paragraph beginning at line 12 with the following rewritten paragraph (which includes the amendments submitted with the Preliminary Amendment filed November 30, 2001):

~~Figure 1 shows~~ Figures 1A, 1B, and 1C show the cDNA (SEQ ID NO:1) sequence and the corresponding deduced amino acid sequence (SEQ ID NO:2) of the G-protein PTH receptor of the present invention. The standard one-letter abbreviation for amino acids is used. Sequencing was performed using a 373 Automated DNA sequencer (Applied Biosystems, Inc.).

On page 6, please replace the paragraph beginning at line 17 and ending on page 7, line 3, with the following rewritten paragraph:

~~Figure 2 is~~ Figures 2A and 2B are an illustration of the secondary structural features of the G-protein PTH receptor. The first 7 illustrations set forth the regions of the amino acid sequence which are alpha helices, beta sheets, turn regions or coiled regions. The boxed areas are the areas which correspond to the region indicated. The second set of figures illustrate areas of the amino acid sequence which are exposed to intracellular, cytoplasmic or are membrane-spanning. The hydrophilicity plot illustrates areas of the protein sequence which are the lipid bilayer of the membrane and are, therefore, hydrophobic, and areas outside the lipid bilayer membrane which are hydrophilic. The antigenic index corresponds to the hydrophilicity plot, since antigenic areas are areas outside the lipid bilayer membrane and are capable of binding antibodies. The surface probability plot further corresponds to the antigenic index and the hydrophilicity plot. The amphipathic plots show those regions of the protein sequences which are polar and non-polar. The flexible regions correspond to the second set of illustrations in the sense that flexible regions are those which are outside the membrane and inflexible regions are transmembrane regions.

On page 7, please replace the paragraph beginning at line 3 with the following rewritten paragraph (which includes the amendments submitted with the Preliminary Amendment filed November 30, 2001):

~~Figure 3 illustrates~~ Figures 3A, 3B, and 3C illustrate an amino acid alignment of the G-protein PTH receptor of the present invention (top line) and the human PTH receptor (bottom line). In ~~Figure 3~~ Figures 3A, 3B, and 3C, the "Query:" line refers to the polypeptide sequence portion of the polypeptide according to the invention and the "Sbjct." line refers to the comparative portions from human PHT receptor protein. Further, in ~~Figure 3~~ Figures 3A, 3B, and 3C, the polypeptide segments set forth in Query:729-908/Sbjct.:253-312; Query:909-1088/Sbjct.:313-372; Query:1089-1244/Sbjct.:373-424; Query:267-446/Sbjct.:102-161; Query:447-476/Sbjct.:162-171; Query:498-677/Sbjct.:177-236; Query:678-740/Sbjct.:237-257; Query:1248-1424/Sbjct.:427-485; Query:159-269/Sbjct.:24-60; and Query:1508-1576/Sbjct.:512-534 correspond to SEQ ID NOS:9-28, respectively.

On page 7, please replace the paragraph beginning at line 7 with the following rewritten paragraph (which includes the amendments submitted with the Preliminary Amendment filed November 30, 2001):

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the mature polypeptide having the deduced amino acid sequence of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:2) or for the mature polypeptide encoded by the cDNA of the clone deposited as ATCC Deposit No. 97186 on June 1, 1995 with the American Type Culture Collection (ATCC) at 10801 University Boulevard, Manassas, VA 20110-2209 under terms of the Budapest Treaty.

On page 7, please replace the paragraph beginning at line 21 with the following rewritten paragraph:

The polynucleotide of the present invention may be in the form of RNA or in the form of DNA, which DNA includes cDNA, genomic DNA, and synthetic DNA. The DNA may be double-stranded or single-stranded, and if single stranded may be the coding strand or non-coding (anti-sense) strand. The coding sequence which encodes the mature polypeptide may be identical to the coding sequence shown in Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:1) or that of the deposited clone or may be a different coding sequence which coding sequence, as a result of the redundancy or degeneracy of the genetic code, encodes the same mature polypeptide as the DNA of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:1) or the deposited cDNA.

On page 7, please replace the paragraph beginning at line 33 and ending on page 8, line 6, with the following rewritten paragraph:

The polynucleotide which encodes for the mature polypeptide of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:2) or for the mature polypeptide encoded by the deposited cDNA may include: only the coding sequence for the mature polypeptide; the coding sequence for the mature polypeptide and additional coding sequence; the coding sequence for the mature polypeptide (and optionally additional coding sequence) and non-coding sequence, such as introns or non-coding sequence 5' and/or 3' of the coding sequence for the mature polypeptide.

On page 8, please replace the paragraphs beginning at line 11 and ending on page 9, line 2, with the following rewritten paragraphs:

The present invention further relates to variants of the hereinabove described polynucleotides which encode for fragments, analogs and derivatives of the polypeptide having the deduced amino acid sequence of ~~Figure 1~~ Figures 1A, 1B, and 1C (SEQ ID NO:2) or the polypeptide encoded by the cDNA of the deposited clone. The variant of the polynucleotide may be a naturally occurring allelic variant of the polynucleotide or a non-naturally occurring variant of the polynucleotide.

Thus, the present invention includes polynucleotides encoding the same mature polypeptide as shown in ~~Figure 1~~ Figures 1A, 1B, and 1C (SEQ ID NO:2) or the same mature polypeptide encoded by the cDNA of the deposited clone as well as variants of such polynucleotides which variants encode for a fragment, derivative or analog of the polypeptide of ~~Figure 1~~ Figures 1A, 1B, and 1C (SEQ ID NO:2) or the polypeptide encoded by the cDNA of the deposited clone. Such nucleotide variants include deletion variants, substitution variants and addition or insertion variants.

As hereinabove indicated, the polynucleotide may have a coding sequence which is a naturally occurring allelic variant of the coding sequence shown in ~~Figure 1~~ Figures 1A, 1B, and 1C (SEQ ID NO:1) or of the coding sequence of the deposited clone. As known in the art, an allelic variant is an alternate form of a polynucleotide sequence which may have a substitution, deletion or addition of one or more nucleotides, which does not substantially alter the function of the encoded polypeptide.

On page 9, please replace the paragraph beginning at line 19 and ending on page 10, line 2, with the following rewritten paragraphs:

The present invention further relates to polynucleotides which hybridize to the hereinabove-described sequences if there is at least 70%, preferably at least 90%, and more preferably at least 95% identity between the sequences. The present invention particularly relates to polynucleotides which hybridize under stringent conditions to the hereinabove-described polynucleotides. As herein used, the term "stringent conditions" means hybridization will occur only if there is at least 95% and preferably at least 97% identity between the sequences. The polynucleotides which hybridize to the hereinabove described polynucleotides in a preferred embodiment encode polypeptides which either retain substantially the same biological function or activity as the mature polypeptide encoded by the cDNAs of Figure 1 Figures 1A, 1B, and 1C (SEQ ID NO:1) or the deposited cDNA(s), i.e. function as a soluble PTH receptor by retaining the ability to bind the ligands for the receptor even though the polypeptide does not function as a membrane bound PTH receptor, for example, by eliciting a second messenger response.

On page 11, please replace the paragraphs beginning at line 14 and ending on page 12, line 14, with the following rewritten paragraphs:

The present invention further relates to a PTH receptor polypeptide which has the deduced amino acid sequence of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:2) or which has the amino acid sequence encoded by the deposited cDNA, as well as fragments, analogs and derivatives of such polypeptide.

The terms "fragment," "derivative" and "analog" when referring to the polypeptide of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:2) or that encoded by the deposited cDNA, means a polypeptide which either retains substantially the same biological function or activity as such polypeptide, i.e. functions as a PTH receptor, or retains the ability to bind the ligand for the receptor even though the polypeptide does not function as a G-protein PTH receptor, for example, a soluble form of the receptor.

The polypeptide of the present invention may be a recombinant polypeptide, a natural polypeptide or a synthetic polypeptide, preferably a recombinant polypeptide.

The fragment, derivative or analog of the polypeptide of Figure 1- Figures 1A, 1B, and 1C (SEQ ID NO:2) or that encoded by the deposited cDNA may be (i) one in which one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code, or (ii) one in which one or more of the amino acid residues includes a substituent group, or (iii) one in which the mature polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol), or (iv) one in which the additional amino acids are fused to the mature polypeptide which are employed for purification of the mature polypeptide or a proprotein sequence or (v) one in which a fragment of the polypeptide is soluble, i.e. not membrane bound, yet still binds ligands to the membrane bound receptor. Such fragments, derivatives and analogs are deemed to be within the scope of those skilled in the art from the teachings herein.